

AMENDMENTS TO THE SPECIFICATION

Please amend the specification on page 2, line 15 to page 3, line 10 as follows:

0-15% of nosocomial (hospital acquired) infections are due to *Pseudomonas aeruginosa*, with 2 million cases annually in the US alone. In some situations, the frequency is even higher. Of around 150,000 burn patients treated in US hospitals and burn centres per year, 26% have *Pseudomonas aeruginosa* infections. *Pseudomonas aeruginosa* is notorious for its resistance to antibiotics so infections caused by it can be difficult to treat. One of its natural habitats is soil, where it is exposed to organisms that produce antibiotics. This may well have led to the development of resistance mechanisms coded for both by genes on the chromosome and by transferable genetic elements known as plasmids. The properties of the *P. aeruginosa* outer membrane are important in conferring resistance. An additional resistance mechanism is its tendency to grow on available surfaces as complex layers known as biofilms [Donlan (2002) *Emerging Infectious Diseases* 8: 881-890, <http://www.cdc.gov/ncidod/EID/vol8no9/02-0063.htm>; Fletcher & Decho (2001) *Biofilms in Encyclopaedia of Life Sciences*, Nature Publishing, London; <http://www.els.net>] that are resistant to far higher concentrations of antibiotics than are required to kill individual cells [Chen et al (2002) *Pseudomonas* infection; <http://www.emedicine.com/PED/topic2701.htm>; Qarah et al (2001) *Pseudomonas aeruginosa* infections; <http://www.emedicine.com/MED/topic1943.htm>; Todar K. (2002) *Todar's Online Textbook of Bacteriology: Pseudomonas aeruginosa*; <http://textbookofbacteriology.net/pseudomonas.html>; Iglewski B. H (1996) *Pseudomonas*. *Medical Microbiology* 4th edition, S. Baron (ed.). University of Texas; <http://gsbs.utmb.edu/microbook/ch027.htm>]. The practical effect of this is demonstrated by infections in cystic fibrosis patients, virtually all of whom eventually become infected with a bacterial strain that cannot be eradicated by the use of antibiotics, even when the isolated strain may appear to be sensitive in the laboratory [Hoiby N (1998) *Pseudomonas* in cystic fibrosis: past, present, future. *European Cystic Fibrosis Society Joseph Levy Memorial Lecture*; http://www.ecfsoc.org/pa_review/nh_lect.html].

Please amend the specification on page 4, lines 13 to 28 as follows:

In addition to the biofilm problem, only a few antibiotics in any case are capable of effective action against *Pseudomonas aeruginosa*, including fluoroquinolones, gentamicin and

imipenem, and even these antibiotics are not effective against all strains. Multidrug resistance is common and increasing [Friedland I et al (2003). *Diagnostic Microbiology and Infectious Disease* 45:245-50; Henwood et al (2001). *Journal of Antimicrobial Chemotherapy* 47: 789-799]. The U.S. National Nosocomial Infections Surveillance System Report of June 1999 [Gerberding J et al (2001). *National Nosocomial Infections Surveillance (NNIS) System Report, data summary from January 1992-June 2001, issued August 2001. U.S. Department of Health and Human Services, Atlanta, http://www.cdc.gov/nceidod/hip/NNIS/2001nnis_report.PDF] states that antibiotic resistance of *Pseudomonas aeruginosa* isolated from nosocomial infections in ICU patients in 1999 had increased over the 1994-98 period for all classes of antibiotics studied. There is therefore a demonstrated need for new approaches to the control of *Pseudomonas aeruginosa* infection. The inventors in this instance have addressed this problem through use of new bacteriophage-based therapies.*

Please amend the specification on page 16, lines 2 to 19 as follows:

Software for performing BLAST analyses is publicly available through the National Centre for Biotechnology Information (<http://www.ncbi.nlm.nih.gov/>). This algorithm involves first identifying high scoring sequence pair (HSPs) by identifying short words of length W in the query sequence that either match or satisfy some positive-valued threshold score T when aligned with a word of the same length in a database sequence. T is referred to as the neighbourhood word score threshold (Altschul et al, supra). These initial neighbourhood word hits act as seeds for initiating searches to find HSPs containing them. The word hits are extended in both directions along each sequence for as far as the cumulative alignment score can be increased. Extensions for the word hits in each direction are halted when: the cumulative alignment score falls off by the quantity X from its maximum achieved value; the cumulative score goes to zero or below, due to the accumulation of one or more negative-scoring residue alignments; or the end of either sequence is reached. The BLAST algorithm parameters W, T and X determine the sensitivity and speed of the alignment. The BLAST program uses as defaults a word length (W) of 11, the BLOSUM62 scoring matrix (see Henikoff and Henikoff (1992) *Proc. Natl. Acad. Sci. USA* 89: 10915-10919) alignments (B) of 50, expectation (E) of 10, M=5, N=4, and a comparison of both strands.